(IL-1b, IL-6, IL-8, IFN-γ, MIF and TNF-α). We have observed clinical differences in the rates of mixed chimerism and GVHD depending on when the alemtuzumab is given. This data suggests that the cytokine milieu may contribute to the development of GVHD and Transplant Related Morbidity (TRM).

398

OUTCOMES OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN COMMUNITY CANCER CENTERS: SINGLE INSTITUTION EXPERIENCE

Khaled, Y., Beredo, L., McEntee, S., Fondaw, M., Villegas, M., Mountford, K., Reddy, V. Florida Cancer Institute, Orlando, FL

Variability in outcomes after hematopoietic stem cell transplantation (HCT) due to differences in health care delivery is traditionally referred to as "center effect". Data analysis by CIBMTR demonstrated improved day 100 survival after related donor (RD) HCT with greater physician involvement in patient's care regardless of medical school affiliation. We hypothesized that the greater physician involvement in patient's care at our community transplant center would compensate for the lack of infrastructure available to academic centers and result in comparable outcomes. We retrospectively reviewed the medical records of 50 consecutive patients who underwent matched unrelated (MUD) HCT (n = 26) or RD HCT (n = 24) for hematological malignancies between August 2007 and April 2010. GVHD prophylaxis used was Tacrolimus/Methotrexate or Tacrolimus/Mycophenolate. MUD HCT recipients recieved ATG in addition. Twenty one (42%) and twenty eight patients (56%) of cohort had progressive/persistent disease and high risk cytogenetics at time of transplant respectively. Thirty three patients (66%) had Charlson Co-morbidity index of 3 or more. Patients characteristic is shown in the table below.

Table 1. Patients characteristic

Number of patients	50 (100%)
Age	Median 56 (Range 23-71)
Patients above the age of 55	27 (54%)
Patients below the age of 55	23 (46%)
Match related (RD)	23 (46%)
Mismatched related 5/6	1 (2%)
Matched unrelated (MUD)	22 (44%)
Mismatched unrelated	4 (8%)
Male	30 (60%)
Female	20 (40%)
Diagnosis	
AML/MDS	26 (52%)
ALL	8 (16%)
Myelofibrosis	2 (4%)
CLL	2 (4%)
T-cell prolymphocytic leukemia	2 (4%)
CML (accelarated phase)	1 (2%)
HD	2 (4%)
Severe aplastic anemia	1 (2%)
Non Hodgkins lymphoma	3 (6%)
Multiple myeloma	3 (6%)
Stem cell source	Peripheral stem cells 50 (100%)
Status at transplant	
Complete remission -1	20 (40%)
Complete remission-2	9 (18%)
Progressive disease	7 (14%)
Persistent disease	14 (28%)
Prior Transplants	
Autologous	7; non tandem (14%)
Allogeneic related	5 (10%)
Cytogenetics	
High Risk	28 (56%)
Normal	19 (38%)
Not available	3 (6%)
Charlson Comorbidity Index	
Score 0	7 (14%)
Score 1-2	10 (20%)
Score 3-4	20(40%)
Score 5 and above	13 (26%)
Conditioning Regimens	
Full Intensity (FIC)	20 (40%)
Reduced Intensity(RIC)	21(42%)
Non Myeloablative (NMA)	9 (18%)

GVHD, graft versus host disease; OS, overall survival; DFS, disease free survival; NRM, non relapse mortality; NMA, Flu/TBI, RIC, FluBU-2/Flu-Mel, FIC FluBU-4/BUCY/CYTBI

OS at 100 days and 1 year were 86% and 67% respectively. There was no statistical difference in OS between RD and MUD; (83% vs. 88% at day 100 and 74% vs. 64% at 1 year for RD and MUD recipients respectively, $P = 0.85$). DFS was 55% at 1year. Again, there was no statistical significance difference in DFS between RD and MUD at 1 year ($P = 0.48$). The cumulative incidence of relapse was 16% at 1 year (21% for RD and12% for MUD). We found no difference in the cumulative incidence of NRM between RD and MUD recipients at day 100 (12%). In contrast, NRM was higher at 1 year in MUD recipients of 34% vs. 25% for the RD recipients. The overall cumulative incidence of acute GVHD grade II-IV was 47.8% with incidence of severe GVHD grade III/IV of 16%. The cumulative incidence of chronic GVHD was 67.6%.

Conclusions: Allogeneic HCT outcomes in the community seem to be comparable to outcomes reported in literature. In this single institution experience, despite the absence of direct cause and effect relationship, the greater involvement of physicians in the patient's care may have contributed to the improved outcomes in this high risk cohort of patients. Community transplant centers may contribute in the future to meet the increased demands for allogeneic HCT with reasonable outcomes.

399

PRELIMINARY RESULTS OF PHASE II TRIAL OF CLOFARABINE WITH PARENTERAL BUSULFAN (CLO/BU) FOLLOWED BY ALLOGENEIC RELATED OR UNRELATED DONOR TRANSPLANTATION FOR THE TREATMENT OF HEMATOLOGIC MALIGNANCIES

Agura, E.[1,2], Berryman, R.B.[1,2], Pineiro, L.[1,2], Vance, E.[1,2], Tadic-Ovcina, M.[1], Woelfel, R.G.[1], Fay, J.[1,2] [1]Charles A Sammons Cancer Center, Baylor University Medical Center, Dallas, TX; [2]Charles A Sammons Cancer Center, Texas Oncology P.A., Dallas, TX

BACKGROUND: RIT regimens are common, but relapse remains a problem. We proposed and tested a mid-intensity regimen using clofarabine (CLO) with busulfan (BU). We hypothesized this combo would be well tolerated and offer greater anti-leukemic efficacy than existing RIT regimens.

METHODS: We enrolled 20 patients on this single IST, with AML (10), ALL (1), CLL (1), MDS (2) and MDS-AML (6). 15 patients had prior therapies. The regimen was: CLO 40mg/m2 iv daily x5, BU 3.2 mg/kg iv daily x2, followed by 1 rest day, followed by HSCT. Donors were matched at A, B, C, DR, DQ using DNA SBT or mid-res DNA typing. Mismatch ≤ 1 antigen was allowed. GVHD prophylaxis was FK506 and MTX 5mg/m2 iv (d 1,3,6).

RESULTS: Endpoints included toxicity, engraftment, incidence/severity of AGVHD, and disease response.

All patients experienced grade 4 hem tox. Median time to ANC recovery (18/20 patients used GCSF) was 13 days (d9 - d17). Engraftment (> 80% donor chim. at d30) occurred in all patients by FISH and/or STR. Selected tox. included; 2 patients - hand/foot syndrome (1 Gr. 3, REL.); 1 resp. failure (Gr. 3 poss. REL) resolved completely; 5 patients - elevated ALT/AST (Gr.3-4, REL) resolving at regimen completion; other tox. were ≤ Gr. 2. TRM was non-existent in this study.

18 patients developed AGVHD by d100 – 83% grade 1-2; 17% grade 3-4. No deaths attributed to AGVHD following study regimen.

Disease responses are: 11 (58%) patients, in relapse/active disease prior to CLO/BU, achieved CR by d30. 7 (37%) patients in CR at study entry, remained so at d30. 1 patient was N/E for disease response at d30. 1 patient (w / CLL) achieved CR at d132. 7 (37%) patients relapsed (M. d120 (d60 – d699)). 12 (60%) patients expired (M. d222 (d92 – d438)): cardiac arrest (1, d316); asp. pneumonia (1, d158); TTP (1, d438); AGVHD - post DLI (1, d175); relapse (4, M. d192 (d150 – d415)); persistent disease (1, d161); MSOF (1, d92); ITP (1, d307); Pulmonary Embolus (1, d233). Of 19 evaluable patients, 6 (32%) remain in remission with a median follow up of 946 days (31 months) (d396 – d1236).

CONCLUSIONS: CLO/BU is a mid-intensity allo HSCT regimen with promising anti-leukemic efficacy that seems to be well tolerated without significant cardiac, renal or pulmonary toxicities. CLO/BU resulted in full engraftment by day 30 in all patients. Enrolment is closed; data collection/analysis is ongoing to determine the practicality of this regimen being studied in a multicenter comparative clinical trial.

400

MYELOABLATIVE CONDITIONING WITH INTRAVENOUS BUSULPHAN IN A SINGLE DAILY DOSE AND FLUDARABINE (BUF) FOR HLA-IDENTICAL SIBLING ALLOGENEIC HSCT IN MYELOID MALIGNANCIES

De la Serna, J.[1], Bermudez, A.[2], Sanz, J.[3], Caballero, D.[4], De la Cámara, R.[5], Vallejo, C.[6], Serrano, D.[7], Moraleda, J.M.[8], Benlloch, L.[9], Sanz, G.[3] [1]Hospital 12 de Octubre, Madrid, Spain; [2]Hospital Valdecilla, Santander, Spain; [3]Hospital La Fe, Valencia, Spain; [4]Hospital Clinico, Salamanca, Spain; [5]Hospital de la Princesa, Madrid, Spain; [6]Hospital Central, Asturias, Spain; [7]Hospital G. Marañon, Madrid, Spain; [8]Hospital V. Arrixaca, Murcia, Spain; [9]GETH, Spain

Background: There is a need to improve the conditioning regimens for allogeneic HSCT, reducing the regimen related toxicity while maintaining the anti-leukemic effect. The combination of myeloablative doses of intravenous busulphan (BU) with fludarabine (F) has been utilized with an improved safety profile.
Objective: We aimed to test the efficacy and safety of this combination (BUF), with a single daily dose of BU, since prior pharmacologic and clinical studies support its safety compared with standard 4-daily doses.
Patients: Sixty seven consecutive adult patients undergoing HLA identical sibling allogeneic HSCT for myeloid malignancies were recruited from eight Spanish institutions. Their main characteristics are shown in table 1.

Table 1. Patients characteristics

PATIENTS	67
Age: median (range) years	45 (17-74)
Patients aged > 55 years	30%
Male gender	58%
DISEASE	
AML	35 (52.2%)
MDS Intermediate/High risk	21 (31.3%)
Secondary AML	5 (7.5%)
Myeloproliferative disorder	6 (9%)

Conditioning regimen consisted in BU, one daily IV infusion (3.2 mg/kg/d) for 4 days (total dose 12.8 mg/kg), combined with F, 40 mg/m2 daily (total dose 160 mg/m2). GVHD prophylaxis consisted in cyclosporine and methotrexate. Antimicrobial and other supportive measures were followed at each institution policies. Donor graft source was PB in 76% and BM in 24% of cases. Median CD34 cells infused were 4.0 mill/kg (0.6-17).
Results: All but one patient engrafted, with a median of 14 days (8-34) for 0.5 granulocytes and 12 days (7-46) for 20 platelets. Main toxicities (Bearman) were grade 1. Major toxicity was mucositis (Grade 2 or 3, 38% of cases). There were 3 grade-2 VOD cases (4.5%) which resolved. Acute GVHD grade 2-4 incidence was 22%. Day-100 accumulated mortality was 4.5%. The median follow-up of this ongoing study is 14 months (3-51). At the time of this interim analysis, the relapse free survival is 79.8% and overall survival 80.7%. Major causes of death were relapse (59%) and infection or toxicity (35%).

In conclusion, in the HLA identical allogeneic HSCT setting BUF provides excellent tumour control and low transplant related toxicity and mortality. In particular, the incidence of VOD is < 5%.

401

IMPACT OF INJECTION VOLUME AND INFUSION RATE IN A LARGE ANIMAL MODEL DESIGNED TO OPTIMIZE INTRABONE TRANSPLANTATION OF HEMATOPOIETIC STEM CELLS

Pantin, J.M.[1], Robert, H.F.[2], Chen, M.Y.[3], Timothy, H.[2], Randall, C.R.[2], Childs, R.W.[1] [1]National Institutes of Health, Bethesda, MD; [2]National Institutes of Health, Bethesda, MD; [3]National Institutes of Health, Bethesda, MD

Background: The intrabone (IB) route of stem cell administration results in improved engraftment in murine models of transplantation. However, human clinical trials have yet to establish that hematopoietic stem cell (HSC) engraftment is improved with the use of IB delivery. The use of IB vascular access can rapidly restore systemic blood volume and pressure in shock situations, although this access route can be associated with pulmonary emboli. Furthermore, both pressure and shear stress, which have not been characterized with conventional IB delivery techniques, may damage HSCs compromising their ability to engraft. Murine models do not have comparative anatomy or physiology to predict the dynamics of HSC delivery in humans following IB injection. In contrast, swine have similar cardiovascular physiology and size analogous to humans and can be used as a model to study the fluid dynamics of IB injection.
Methods: Forty-five to 60 kg domestic swine were placed under general anesthesia with IB access of the pelvis achieved using an On-Control driver (Vidacare). Isovue was injected into the pelvis at varying volumes and rates and the entire pelvis was imaged by 320-slice ultrafast continuous dynamic CT (Toshiba Aquilion). Pulmonary artery, carotid artery and intramarrow cavity pressures were monitored continuously both during and after injection into the pelvis.
Results: We first characterized the comparative vascular anatomy of the porcine pelvis. The major arterial blood supply to the pelvic bone marrow was found to arise from branches of the internal iliac artery with venous drainage occurring through the iliac vein. IB injection of contrast led to an immediate systemic delivery into the central venous circulation. Reducing the infusion volume and slowing the rate of the infusion both produced smaller increases in IB marrow pressure and post-injection peak pulmonary artery systolic pressure (PASP).

Table 1. Post IB Injection Changes in Intramarrow pressure and Peak PASP

Volume Injected (mL)	Rate Injected (mL/s)	Number of Infusions	Δ Intramarrow Pressure (mmHg) Mean ± S.E.	Δ Peak Pulmonary Artery Systolic Pressure (PASP) (mmHg) Mean ± S.E.
10	0.1	4	159.3 ± 57.7	1.5 ± 0.7
10	0.2	3	300.3 ± 149.3	3.5 ± 1.0
10	0.5	2	803.4 ± 483.0	13.0 ± 5.1
10	1.0	2	1196.0 ± 265.5	8.9 ± 9.3
10	2.5	3	1689.0 ± 116.0	2.2 ± 1.0
5	0.1	2	128.7 ± 60.2	-0.5 ± 0.4
5	0.2	2	256.7 ± 42.7	1.3 ± 1.3
5	0.5	1	802.9	6.1
5	1.0	1	1490.8	0
5	2.5	1	997.5	2

Conclusions: The IB route of injection provides rapid access to the central venous circulation. Increasing IB infusion volumes and/or IB infusion rates led to profound increases in intramarrow pressures and significantly increases PASP. These data suggest continuous monitoring of IB pressures is necessary for studies aimed at characterizing stem cell trafficking and to optimize the retention of HSC in the intrabone marrow space following IB injection.

402

VARICELLA ZOSTER REACTIVATION AFTER CORD BLOOD TRANSPLANTATION: COMPARISON WITH UNRELATED BONE MARROW TRANSPLANTATION

Asano-Mori, Y.[1], Nishida, A.[1], Ikebe, T.[1], Ishiwata, K.[1], Nakano, N.[1], Tsuji, M.[1], Yamamoto, H.[1], Izutsu, K.[1], Uchida, N.[1], Masuoka, K.[2], Wake, A.[1], Yoneyama, A.[3], Makino, S.[4], Taniguchi, S.[1] [1]Toranomon Hospital, Tokyo, Japan; [2]Mishuku Hospital, Tokyo, Japan; [3]Toranomon Hospital, Tokyo, Japan; [4]Toranomon Hospital, Tokyo, Japan

Varicella zoster virus (VZV) infection remains an important problem after allogeneic hematopoietic stem cell transplantation, because VZV-related complications including post-herpetic neuralgia